



MANAGEMENT OF THE SMALL RENAL MASS: A GUIDELINES BASED APPROACH

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disclosures



American Urological Association
Kidney Cancer Guideline Committee



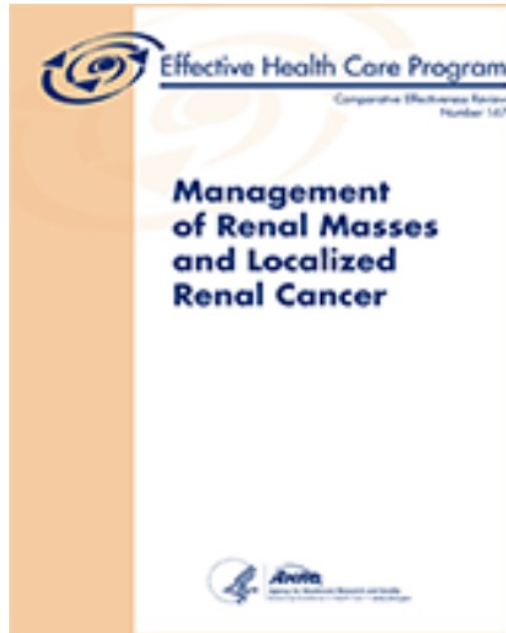
Agency for Healthcare Research and Quality (AHRQ) Funded Investigator
“Management of Renal Masses and Localized Renal Cancer”

No relevant financial relationships to disclose.

Non-FDA approved use of drugs or products discussed in this presentation – NONE.

Latest AUA Guideline Updated in 2021 (2009 then 2017)
Steve Campbell (Chair) and Robert Uzzo (Co-Chair)





Management of Renal Masses and Localized Renal Cancer

Comparative Effectiveness Reviews, No. 167

Investigators: Phillip M Pierorazio, MD, Michael H Johnson, MD, Hiten D Patel, MD, MPH, Stephen M Sozio, MD, MHS, Ritu Sharma, BSc, Emmanuel Iyoha, MBChB, MPH, Eric B Bass, MD, MPH, and Mohamad E Allaf, MD.

► Author Information and Affiliations

Rockville (MD): [Agency for Healthcare Research and Quality \(US\)](#); 2016 Feb.
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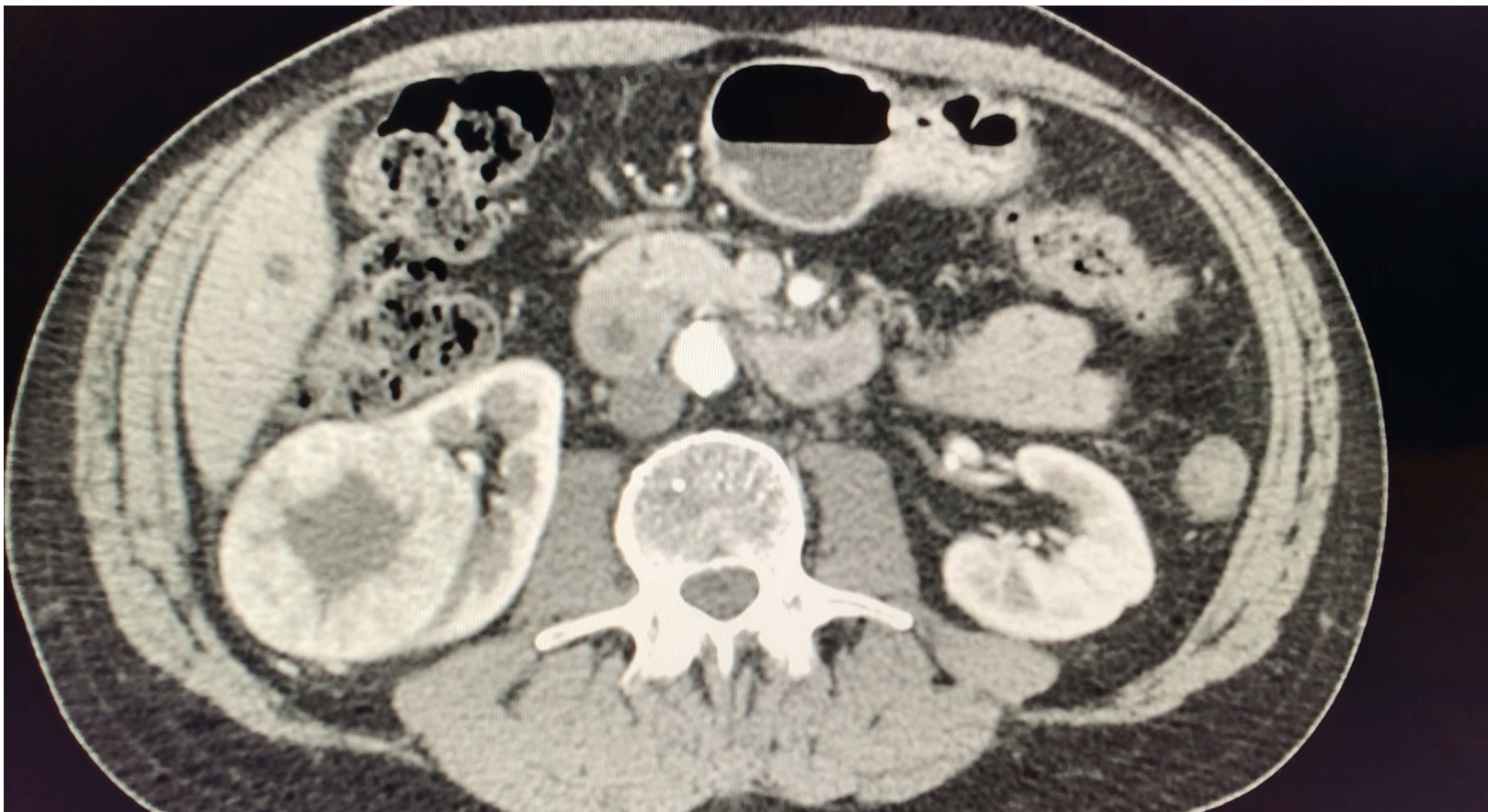


Primary Focus

- Guideline statements focus primarily on **clinically localized sporadic renal masses suspicious for renal cell carcinoma (RCC)** in adults,
 - Solid enhancing renal tumors, and
 - Bosniak 3 and 4 complex cystic renal masses.
 - Bosniak 3 (50% malignant)
 - Bosniak 4 (90% malignant)

Important Updates/Differences from 2009 Guidelines

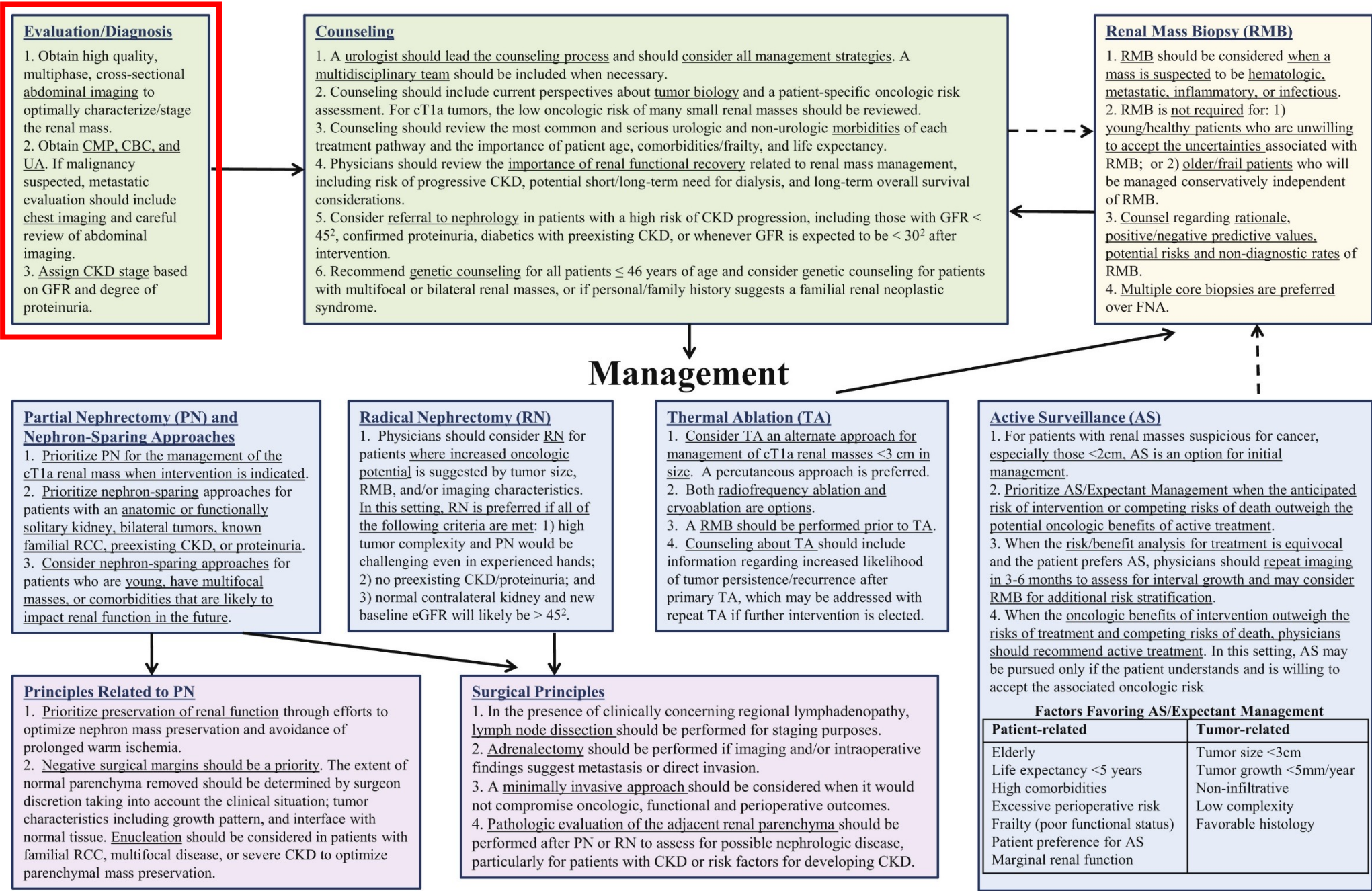
- No index patients. Focus on individual assessment of:
 - Patient characteristics
 - Tumor characteristics
 - Renal functional outcomes
 - Potential harms of each treatment
- Increased focus on renal functional outcomes.
- Clear definitions for the role of partial and radical nephrectomy.
 - Primary role for partial nephrectomy (PN); T1a and otherwise.
 - Restricted role for radical nephrectomy (RN); well-defined selection criteria.
- New perspectives:
 - Renal mass biopsy
 - Thermal ablation
 - Active surveillance



High Quality Multiphase Cross Sectional Abdominal Imaging
Fat? Enhancing? Cystic? Complexity (NEPHROMETRY, PADUA, C-Index)
Chest Imaging for Staging (TIMING AND MODALITY INTENTIONALLY VAGUE)
Assign CKD Stage and Degree of Proteinuria

*Contrast Enhanced MRI if renal insufficiency is safe even in ESRD patients with newer Gadolinium Agents

Renal Mass and Localized Renal Cancer¹



1. Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions. 2. ml/min/1.73m².

Evaluation and Diagnosis:

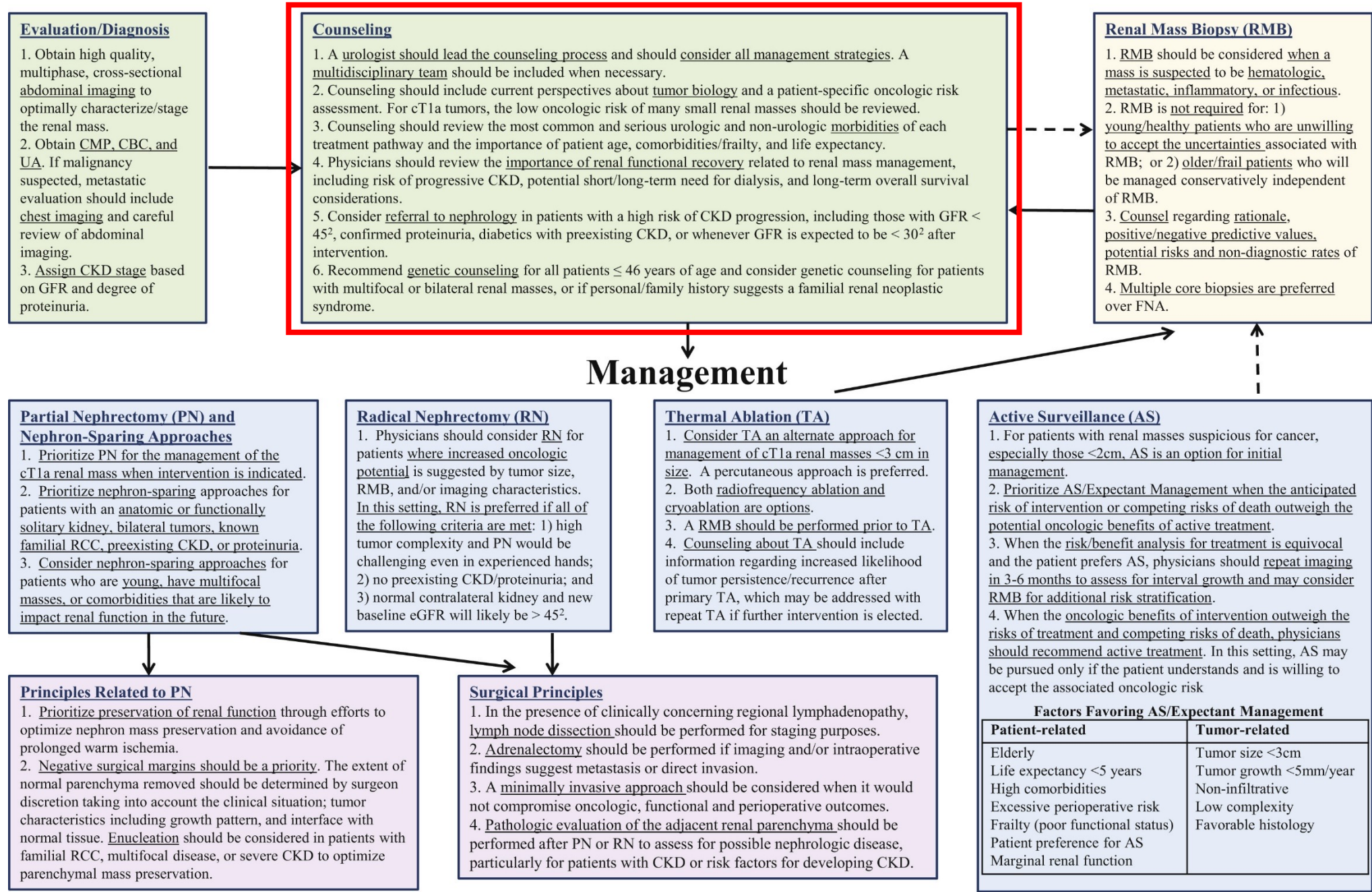
Guideline Statement 3 (**Assessment of Renal Function**)

- For patients with a solid or complex cystic renal mass, physicians should **assign CKD stage** based on GFR and degree of proteinuria. (Expert Opinion)

**Prognosis of CKD by GFR
and Albuminuria Categories:
KDIGO 2012**

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m ²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Renal Mass and Localized Renal Cancer¹



1. Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions. 2. ml/min/1.73m².

Counseling:

Guideline Statement 4 (Team approach)

- In patients with a solid or Bosniak 3/4 complex cystic renal mass, a **urologist should lead the counseling process** and should consider all management strategies.
 - A multidisciplinary team should be included when necessary.(Expert Opinion)

Multidisciplinary Team:

Radiologist

Interventional Radiologist

Pathologist

Nephrologist

Medical Oncologist

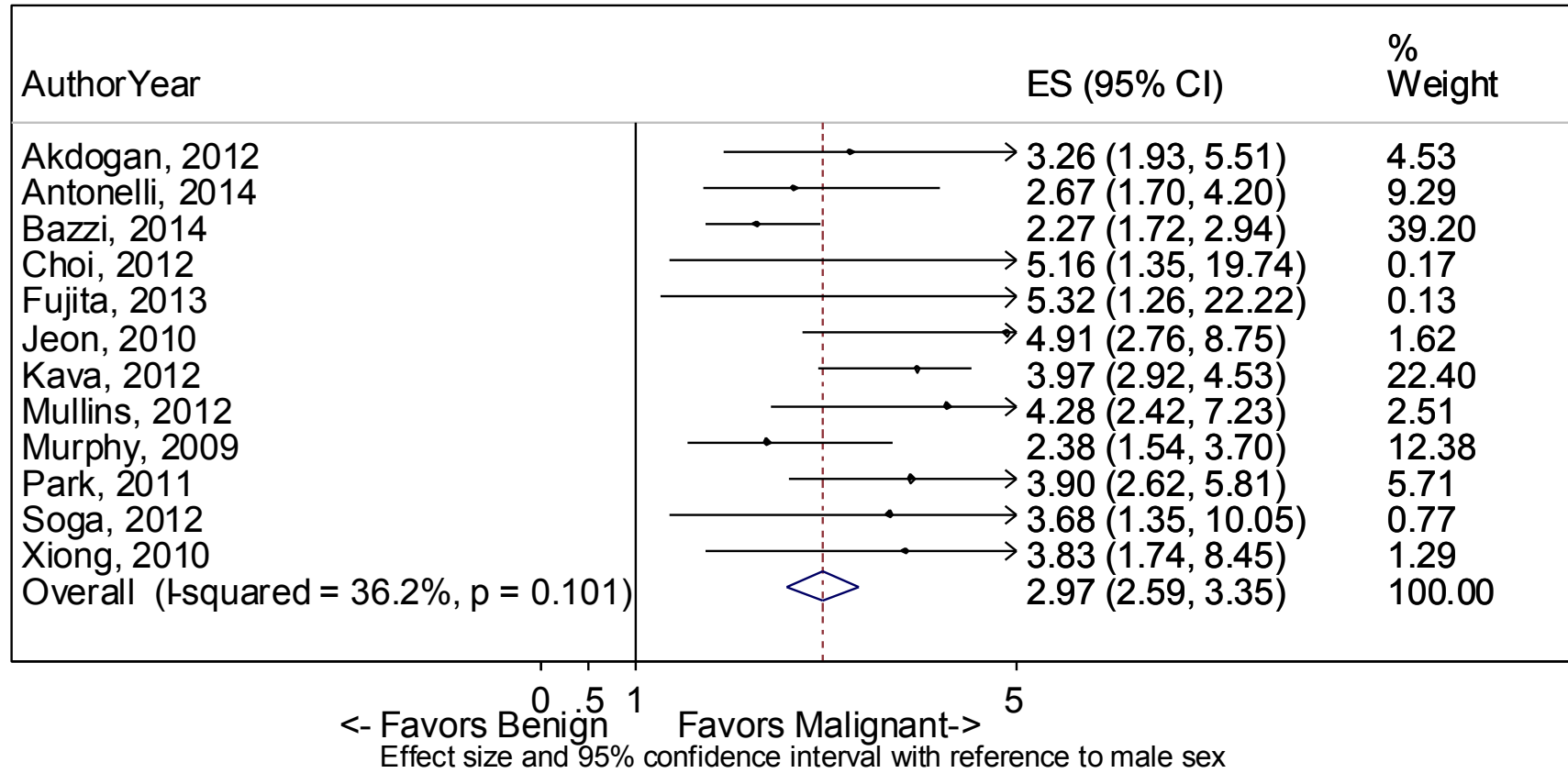
Genetic Counselor



Counseling:

Guideline Statement 5 (**Malignant/Metastatic Potential**)

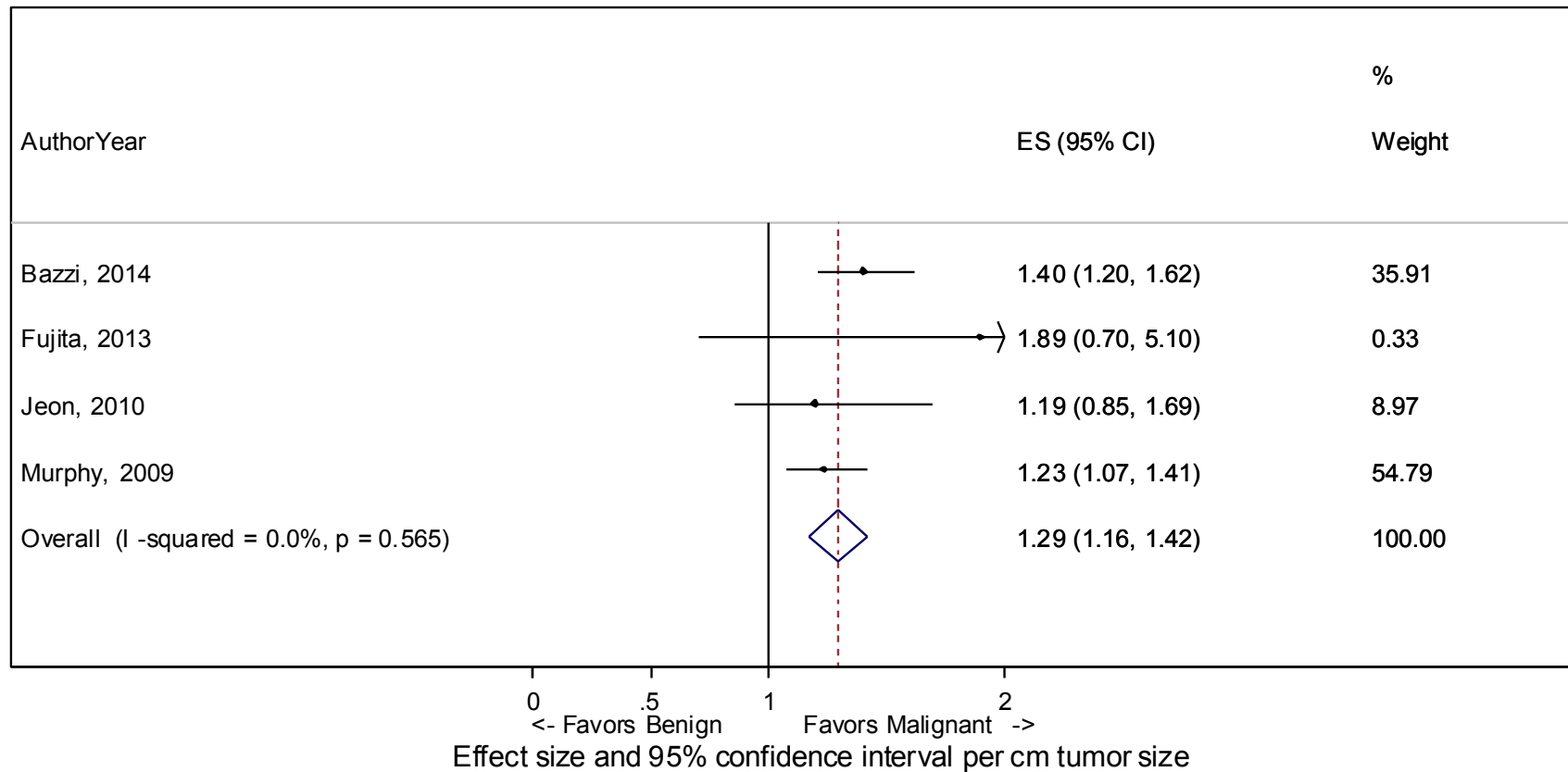
- Physicians should provide counseling that includes current perspectives about **tumor biology and a patient-specific risk assessment** inclusive of sex, tumor size/complexity, histology (when obtained), and imaging characteristics.
 - For cT1a tumors, the low oncologic risk of many small renal masses should be reviewed. (Clinical Principle)



12 of 14 studies demonstrate male sex predicts malignancy

Effect size: 2.97 (95% CI: 2.59 to 3.36)

Moderate strength of evidence.



Increasing tumor size predicts malignancy.

ALL studies of categorical tumor size

Effect size in continuous variable meta-analysis: **1.29 (95% CI: 1.16 to 1.42)**

Moderate strength of evidence.

Original article

Preoperative predictors of malignancy and unfavorable pathology for clinical T1a tumors treated with partial nephrectomy: A multi-institutional analysis

Mark W. Ball, M.D.^{a,*}, Michael A. Gorin, M.D.^a, Sam B. Bhayani, M.D., M.S.^b,
Craig G. Rogers, M.D.^c, Michael D. Stifelman, M.D.^d, Jihad H. Kaouk, M.D.^e,
Homayoun Zargar, M.D.^e, Susan Marshall, M.D.^d, Jeffrey A. Larson, M.D.^b,
Haider M. Rahbar, M.D.^c, Bruce J. Trock, Ph.D.^a, Phillip M. Pierorazio, M.D.^a,
Mohamad E. Allaf, M.D.^a

Predicted risk of RCC and 95% CIs after PN by sex, size, and nephrometry score

	Nephrometry < 8	Nephrometry ≥ 8
Female		
Size < 3 cm	64.0 (58.1–69.7)	74.5 (68.2–80.7)
Size ≥ 3 cm	72.2 (64.6–79.8)	81.0 (75.0–87.1)
Male		
Size < 3 cm	77.0 (72.8–81.2)	84.6 (80.3–89.0)
Size ≥ 3 cm	83.1 (77.9–88.2)	89.0 (85.1–92.8)

Value are listed as risk-estimated percentage (95% CI).

Predicted risk of unfavorable pathology and 95% CIs after PN by sex, size, and nephrometry score

	Nephrometry < 8	Nephrometry ≥ 8
Female		
Size < 3 cm	9.6 (6.6–12.6)	13.7 (8.2–18.1)
Size ≥ 3 cm	13.4 (8.6–18.3)	18.8 (12.7–24.9)
Male		
Size < 3 cm	20.0 (16.0–23.9)	27.1 (21.1–33.1)
Size ≥ 3 cm	26.7 (20.2–33.2)	35.2 (27.8–42.7)

Value are listed as risk-estimated percentage (95% CI).

Counseling:

Guideline Statement 6 (**Comparative Harms**)

- Physicians must review the most common and **serious urologic and non-urologic morbidities of each treatment** pathway and the importance of patient age, comorbidities/frailty, and life expectancy. (Clinical Principle)
- ***Oncologic outcomes are determined by tumor stage.***
- ***Overall survival is determined by competing risks.***
- ***Comparative harms (including renal function) are the greatest variable among management options.***



5-year outcomes	Radical Nephrectomy	Partial Nephrectomy	Thermal Ablation	Active Surveillance
Cancer-specific survival	95.5-99% (IQR 91-100%)	97.8-100% (IQR 94.4-100%)	95.4-96% (IQR 92-98%)	98-100% FU 12-36 months
T1a	97% (IQR 95.7-98.3%)	98.8% (IQR 98.9-100%)		
T1b	91% (IQR 69.6-94.3%)	90% (IQR 80.8-93.8%)		
T2	82.5% (NA)	86.7% (NA)		
Metastasis-free survival	94.8-97.2% (IQR 92.3-100%)	98-99% (IQR 97.1-100)	95.3-97.6% (IQR 90.5-100%)	98-100%
Local recurrence-free survival	98.7-99.6% (IQR 97.4-100%)	98.8-99.4% (IQR 96.4-100%)	87-89.3% 97-100%* (IQR 81-94.7%)	NA
Overall survival	86.3-97% (IQR 76-100%)	92.3-97.8% (IQR 82.7-100%)	70.5-88% (IQR 48-95.3%)	69-94%

Oncologic Outcomes

Pierorazio PM, *et al.* Management of Renal Masses and Localized Renal Cancer (Prepared by the JHU Evidence-based Practice Center under Contract No. HHSA2902012000071.) Rockville, MD: Agency for Healthcare Research and Quality. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.



Comparative Harms

Radical Nephrectomy (RN)	Partial Nephrectomy (PN)	Thermal Ablation (TA)	Active Surveillance (AS)
- greatest decrease in eGFR - highest risk of <i>de novo</i> CKD stage 3 or higher. - favorable perioperative outcomes (high proportion performed laparoscopically) - low risk of urologic complications compared to PN.	- excellent preservation of renal parenchyma and GFR - higher risk (low overall rate) of blood transfusions and urologic complications (e.g. urine leak).	- inferior LRFS (when considering 1' efficacy). - most favorable perioperative outcome. - low risk of overall harms. - success rates with TA are highest with small peripheral tumors.	- favorable oncologic and overall survival outcomes in well-selected patients. - foregoes the operative risks, potentially introduces anxieties and oncologic risks.

It is impossible to make a blanket statement that one management strategy is preferred based on patient age, comorbidities, frailty, and/or life expectancy, but all should be considered during individualized counseling.

Counseling:

Guideline Statement 7-8 (Renal Function Consultation)

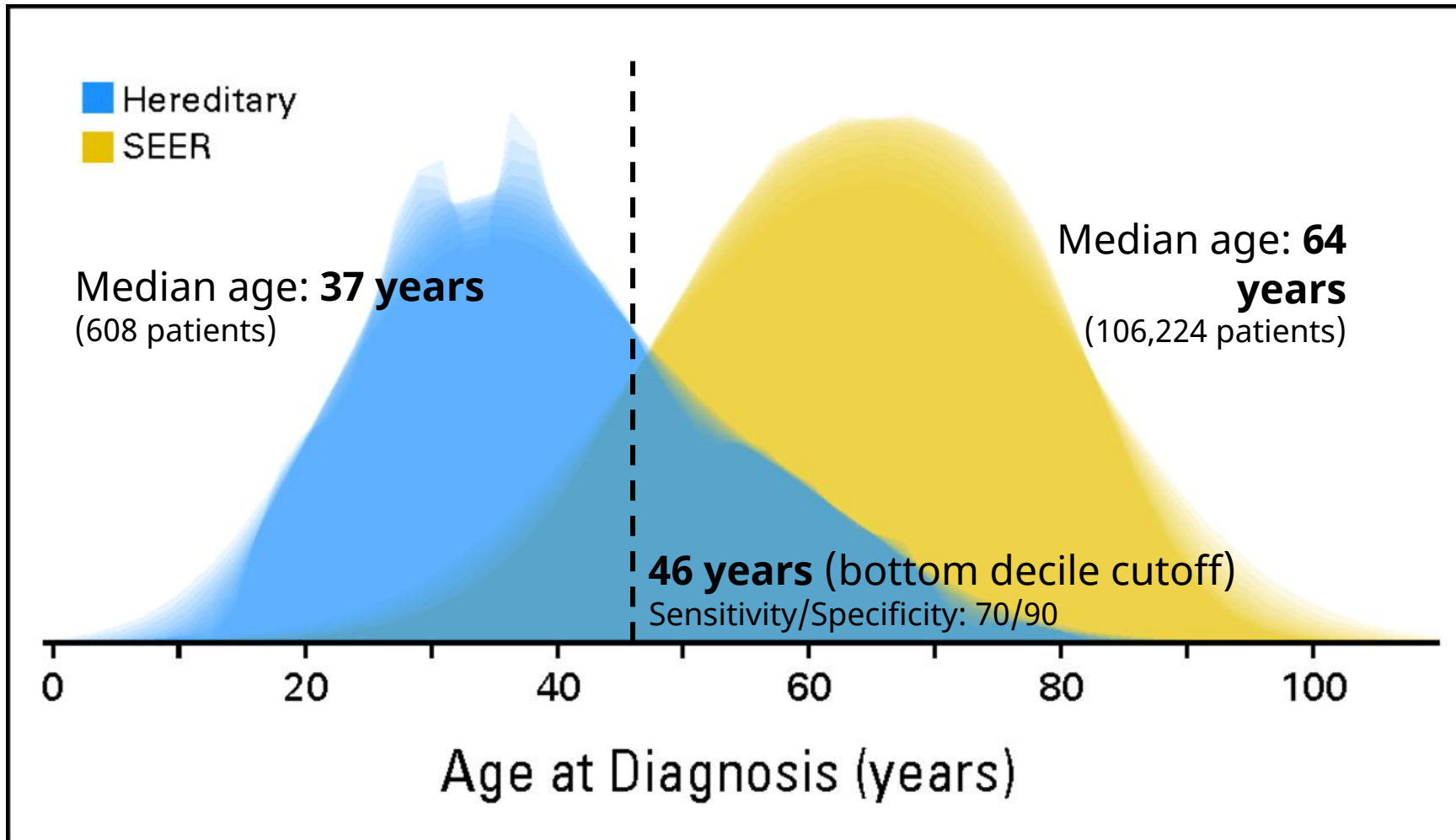
- Physicians should review the importance of **renal functional recovery** related to renal mass management, including the risk of progressive CKD, potential short- or long-term need for renal replacement therapy, and long-term overall survival considerations. (Clinical Principle)
- Physicians should consider **referral to nephrology** in patients with a high risk of CKD progression. Such patients may include those with:
 - eGFR less than 45 ml/min/1.73m²,
 - confirmed proteinuria,
 - diabetics with preexisting CKD, or
 - whenever eGFR is expected to be less than 30 ml/min/1.73m² after intervention.(Expert Opinion)



Counseling:

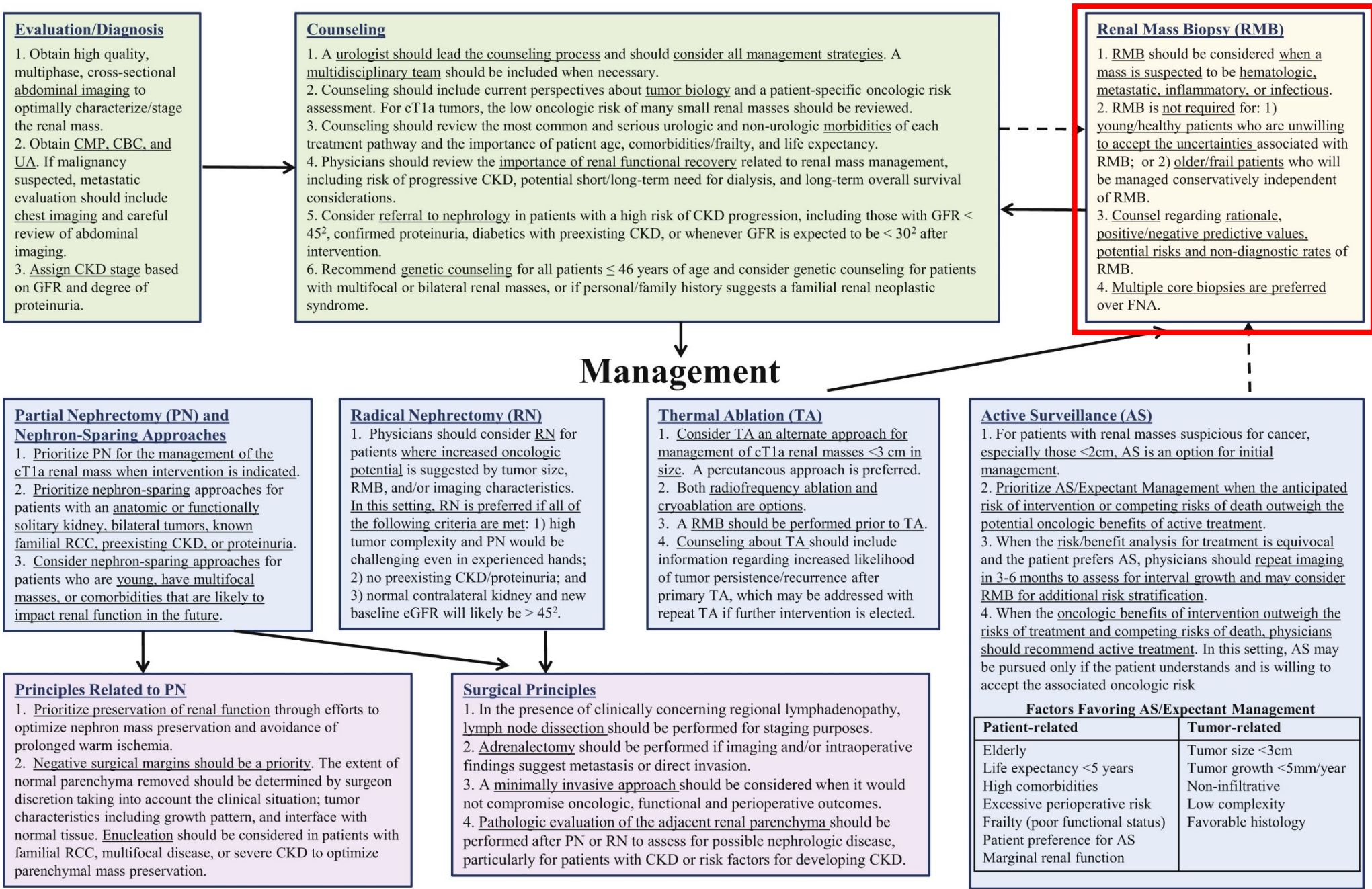
Guideline Statement 9 (Genetic Counseling)

- Physicians should **recommend** genetic counseling for all patients ≤ 46 years of age with renal malignancy, and
- **consider** genetic counseling for patients with:
 - multifocal or bilateral renal masses, or
 - if personal or family history suggests a familial renal neoplastic syndrome.(Expert Opinion)



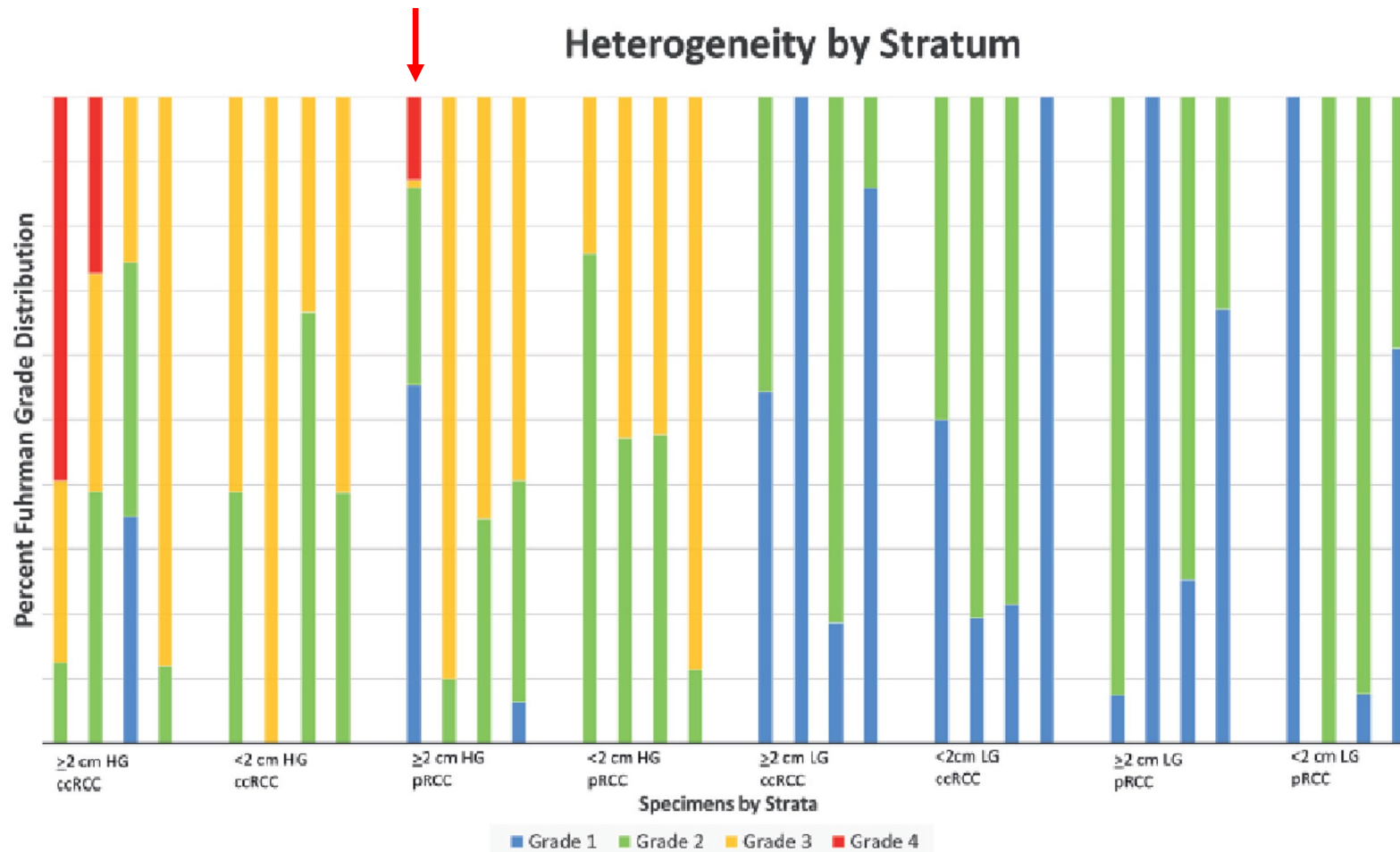
Defining Early-Onset Kidney Cancer: Implications for Germline and Somatic Mutation Testing and Clinical Management
Brian Shuch, et al. Journal of Clinical Oncology 2014 32:5, 431-437

Renal Mass and Localized Renal Cancer¹



Grade Heterogeneity in Small Renal Masses: Potential Implications for Renal Mass Biopsy

Mark W. Ball,^{*,†} Stephania M. Bezerra,[†] Michael A. Gorin,
Morgan Cowan, Christian P. Pavlovich, Phillip M. Pierorazio,
George J. Netto and Mohamad E. Allaf



AUA Guideline: Discussion Points for RMB

- RMB is generally safe with low risk of significant complications (bleeding) and no reported cases of tumor seeding using contemporary techniques.
- A diagnosis of malignancy or RCC on RMB is highly reliable.
- Potential limitations of RMB include:
 - A benign biopsy must be distinguished from a non-diagnostic biopsy (renal parenchyma or connective tissues) result.
 - A benign biopsy may not always correlate with benign histology (NPV).
 - Grade concordance from biopsy to surgically resected tissue is imperfect (50%).
 - Oncocytic neoplasms may represent a diagnostic dilemma.
 - Biopsy or aspiration of cystic renal masses is generally not advised due to concerns regarding tumor spillage and a high likelihood of obtaining a non-informative result due to sampling error.



Surgical Management

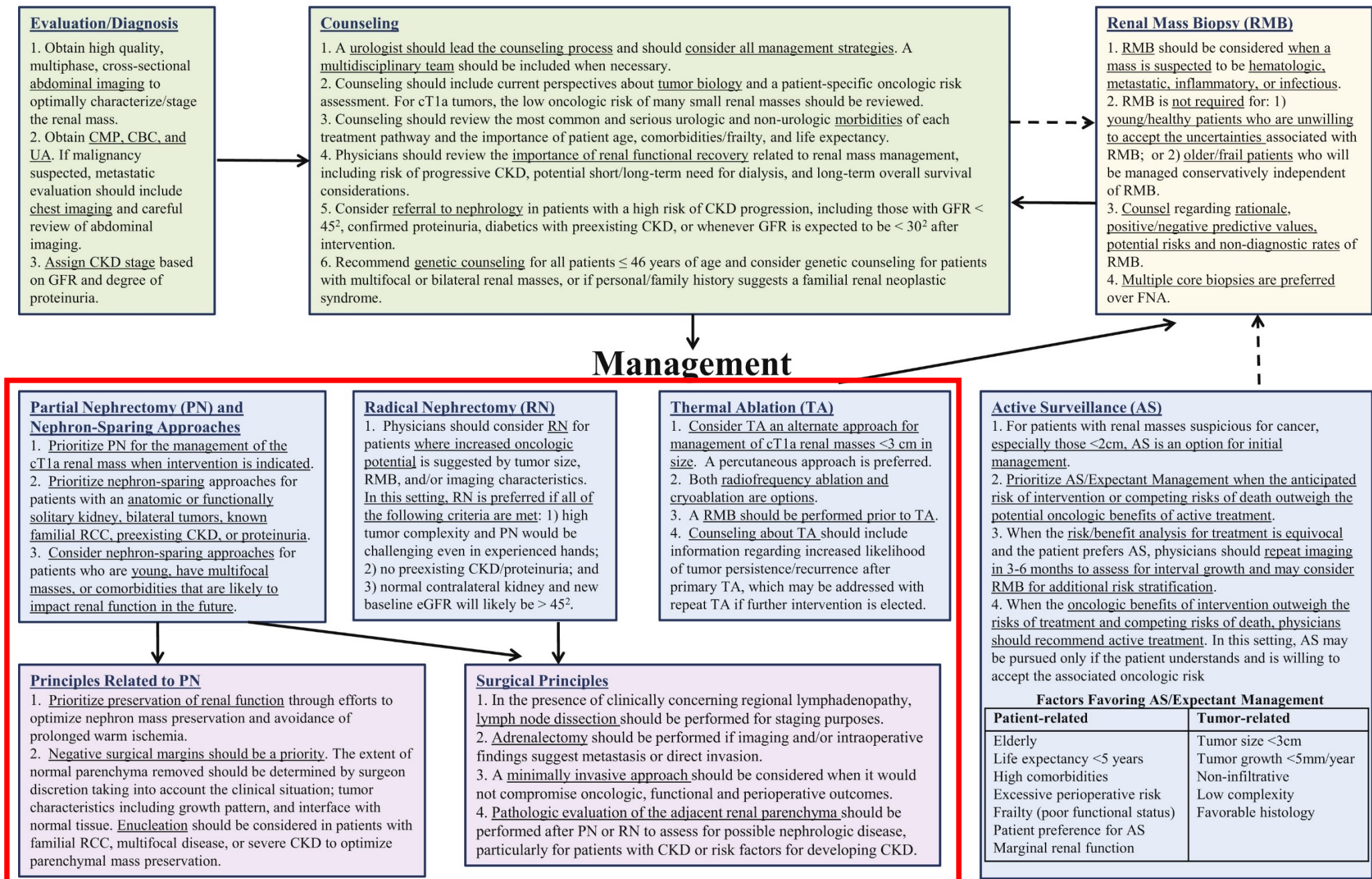
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THE NEW & IMPORTANT



Management BASICS

- Four strategies are considered **standards of care**:
 - Active surveillance,
 - Radical nephrectomy,
 - Partial nephrectomy, and
 - Thermal ablation.
- } Surgical Management
- Other technologies including high intensity focused ultrasound, radiosurgery, microwave therapy, pulsed cavitation ultrasound, and laser thermal therapy remain investigational at this time.

Renal Mass and Localized Renal Cancer¹

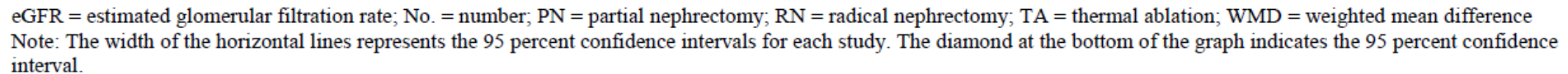


1. Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions. 2. ml/min/1.73m².

Partial Nephrectomy and Nephron-sparing Approaches

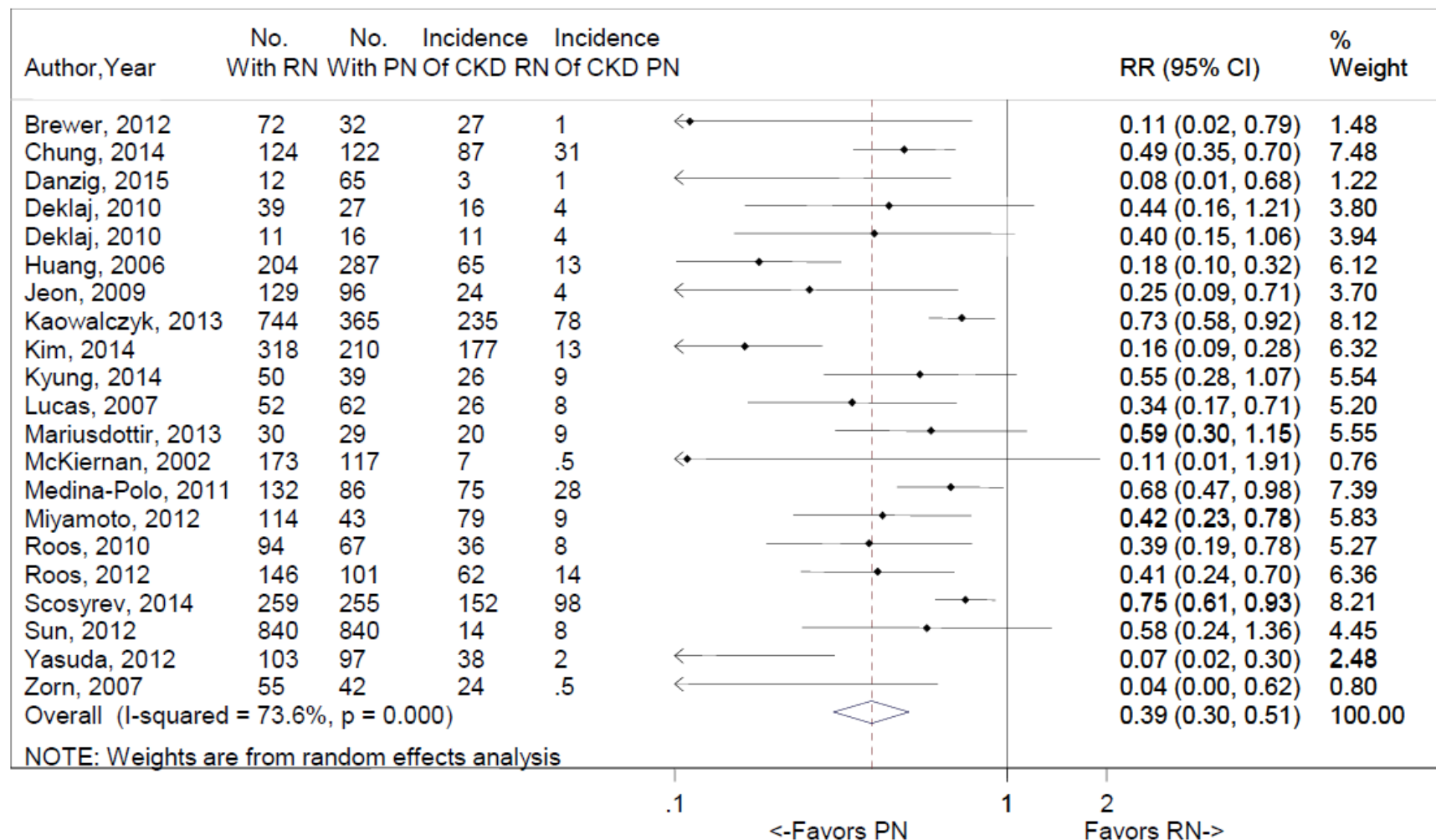
Guideline Statement 14

- Physicians should **prioritize PN** for the management of the cT1a renal mass when intervention is indicated.
 - In this setting, PN minimizes the risk of CKD or CKD progression and is associated with favorable oncologic outcomes, including excellent local control.
- (Moderate Recommendation; Evidence Level: Grade B)



eGFR = estimated glomerular filtration rate; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; TA = thermal ablation; WMD = weighted mean difference
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure 22. Meta-analysis of the incidence of stage 3 chronic kidney disease with radical nephrectomy versus partial nephrectomy



Risk Ratio and 95% Confidence Intervals of Incidence of CKD stage 3

CKD = chronic kidney disease; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; RR = risk ratio; TA = thermal ablation; WMD = weighted mean difference
 Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Partial Nephrectomy and Nephron-sparing Approaches

Guideline Statement 15: “Absolute” Indications

Physicians should **prioritize** nephron-sparing approaches when:

- an anatomic or functionally solitary kidney,
 - bilateral tumors,
 - known familial RCC,
 - preexisting CKD, or proteinuria.
- (Moderate Recommendation; Evidence Level: Grade C)

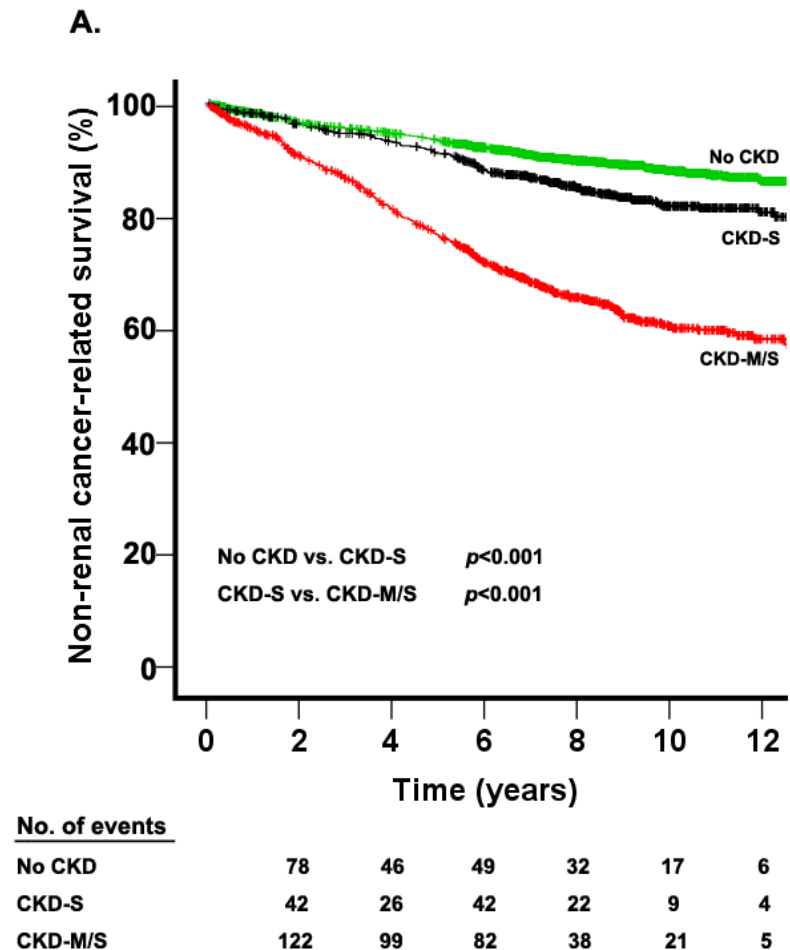
Absolute indications include situations in which RN would render the patient anephric or high-risk for renal replacement therapy (RRT).

While patients with familial RCC have two functional kidneys, they are likely to experience tumor recurrences and require multiple renal interventions throughout their lifetime.

Patients with **bilateral RCC** are more likely to have familial or recurrent RCC.

Patients with pre-existing CKD/proteinuria are at increased risk for progressive CKD and ESRD.

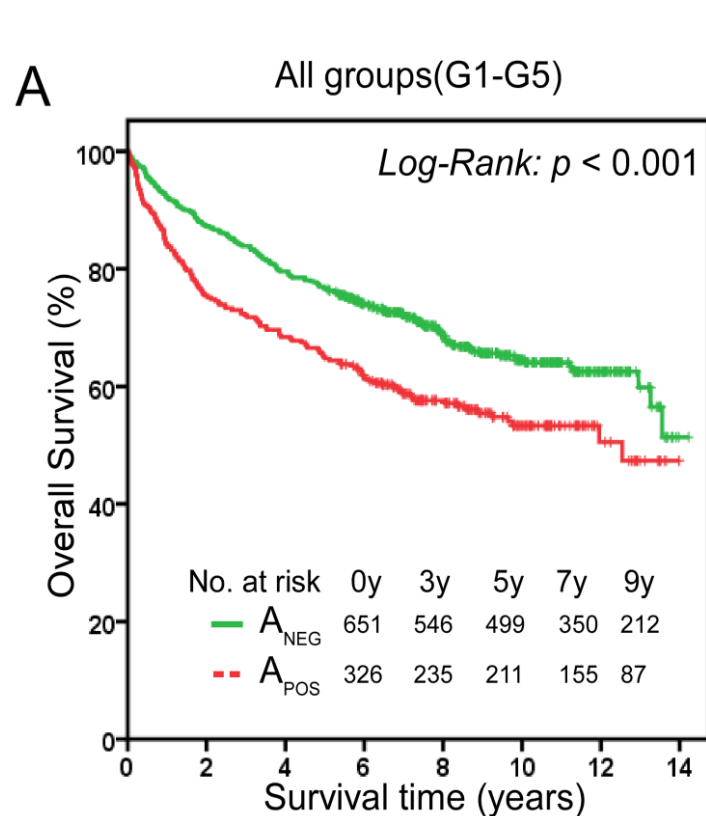
Patients with Preexisting CKD and a Renal Mass: CDK-M/S



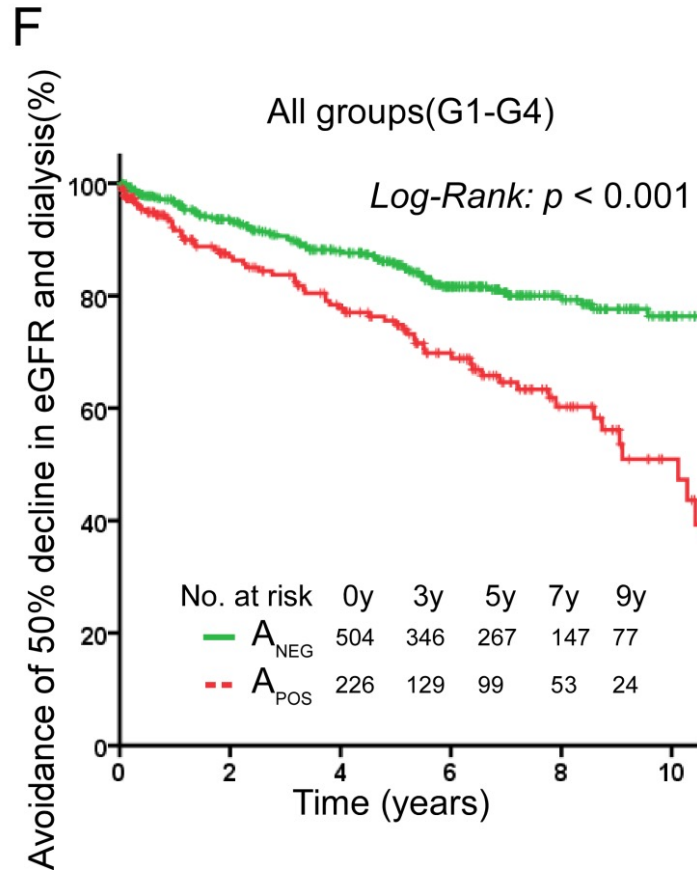
Impact of Proteinuria on Outcomes after Renal Cancer Surgery

Zhang Z, Zhao J, Campbell SC, et al, European Urol Focus (2016):

<http://dx.doi.org/10.1016/j.euf.2016.01.003>



Overall Survival



Stability of Renal Function

No Proteinuria:
Green
+ Proteinuria:
Red

Partial Nephrectomy and Nephron-sparing Approaches

Guideline Statement 17-18 (Technical Considerations)

- In patients who elect PN, physicians should **prioritize preservation of renal function** through efforts to:
 - optimize nephron mass preservation and
 - avoidance of prolonged warm ischemia. (Expert Opinion)
- For patients undergoing PN, **negative surgical margins should be a priority.**
 - The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation, tumor characteristics including growth pattern, and interface with normal tissue.
 - Tumor enucleation should be considered in patients with familial RCC, multifocal disease, or severe CKD to optimize parenchymal mass preservation. (Expert Opinion)



Radical Nephrectomy

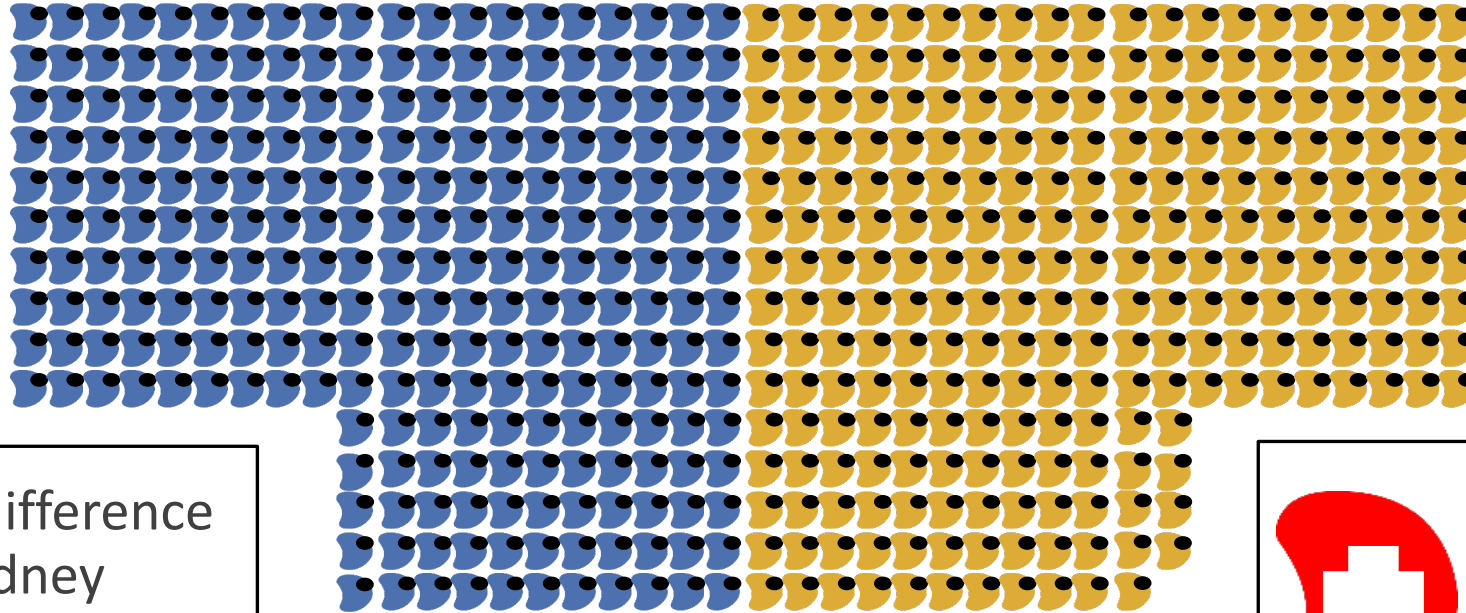
Guideline Statement 19 (“The” RN Statement)

- Physicians should consider RN when **increased oncologic potential** is suggested by:
 - tumor size,
 - renal mass biopsy, and/or
 - imaging characteristics(Conditional Recommendation; Evidence Level: Grade B)
- **AND** in this setting, **RN is preferred** if all of the following criteria are met:
 - 1) high tumor complexity and PN would be challenging even in experienced hands;
 - 2) no preexisting CKD or proteinuria; and
 - 3) normal contralateral kidney and new baseline eGFR will likely be greater than 45 ml/min/1.73m².(Expert Opinion)



European Randomized Study (EORTC 30904)

255 Partial
Nephrectomy



259 Radical
Nephrectomy

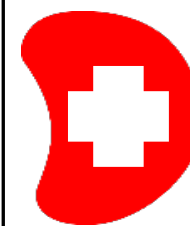


No difference
in kidney
cancer deaths

1992-2003

5cm tumors

All healthy patients



Worse kidney
function after
RN (eGFR), no
difference in
(low) rates of
kidney failure.

Surgical Principles

Guideline Statement 22 (Minimally-invasive Surgery)

- In patients undergoing surgical excision of a renal mass, a **minimally invasive approach** should be considered when it would not compromise oncologic, functional and perioperative outcomes. (Expert Opinion)

*Multiple studies demonstrate recuperative and cosmetic advantages to **laparoscopic RN**.*

***Laparoscopic and robotic PN** have demonstrated equivalent surgical margin status and oncological outcomes when compared to open surgery in well-selected patients.*

*The high rate of **percutaneous TA** may explain the favorable perioperative outcome and harm profile.*

*Minimally-invasive approaches to increasingly complex indications (large renal masses, renal vein thrombi and patients with solitary kidneys) should respect **patient safety and adherence to prior guideline statements**.*



Thermal Ablation

Guideline Statement 24-26 (Indications and Techniques)

- Physicians should consider thermal ablation (TA) as an alternate approach for the management of **cT1a renal masses <3 cm in size**.
 - For patients who elect TA, a percutaneous technique is preferred over a surgical approach whenever feasible to minimize morbidity.
(Conditional Recommendation; Evidence Level: Grade C)
- Both radiofrequency ablation and cryoablation are options for patients who elect thermal ablation. (Conditional Recommendation; Evidence Level: Grade C)
- A renal mass biopsy should be performed prior to ablation to provide pathologic diagnosis and guide subsequent surveillance. (Expert Opinion)



Thermal Ablation

Guideline Statement 27 (TA Counseling)

- Counseling about thermal ablation should include information regarding an **increased likelihood of tumor persistence or local recurrence** after primary thermal ablation relative to surgical extirpation, which may be addressed with repeat ablation if further intervention is elected.

(Strong Recommendation; Evidence Level: Grade B)



Active Surveillance

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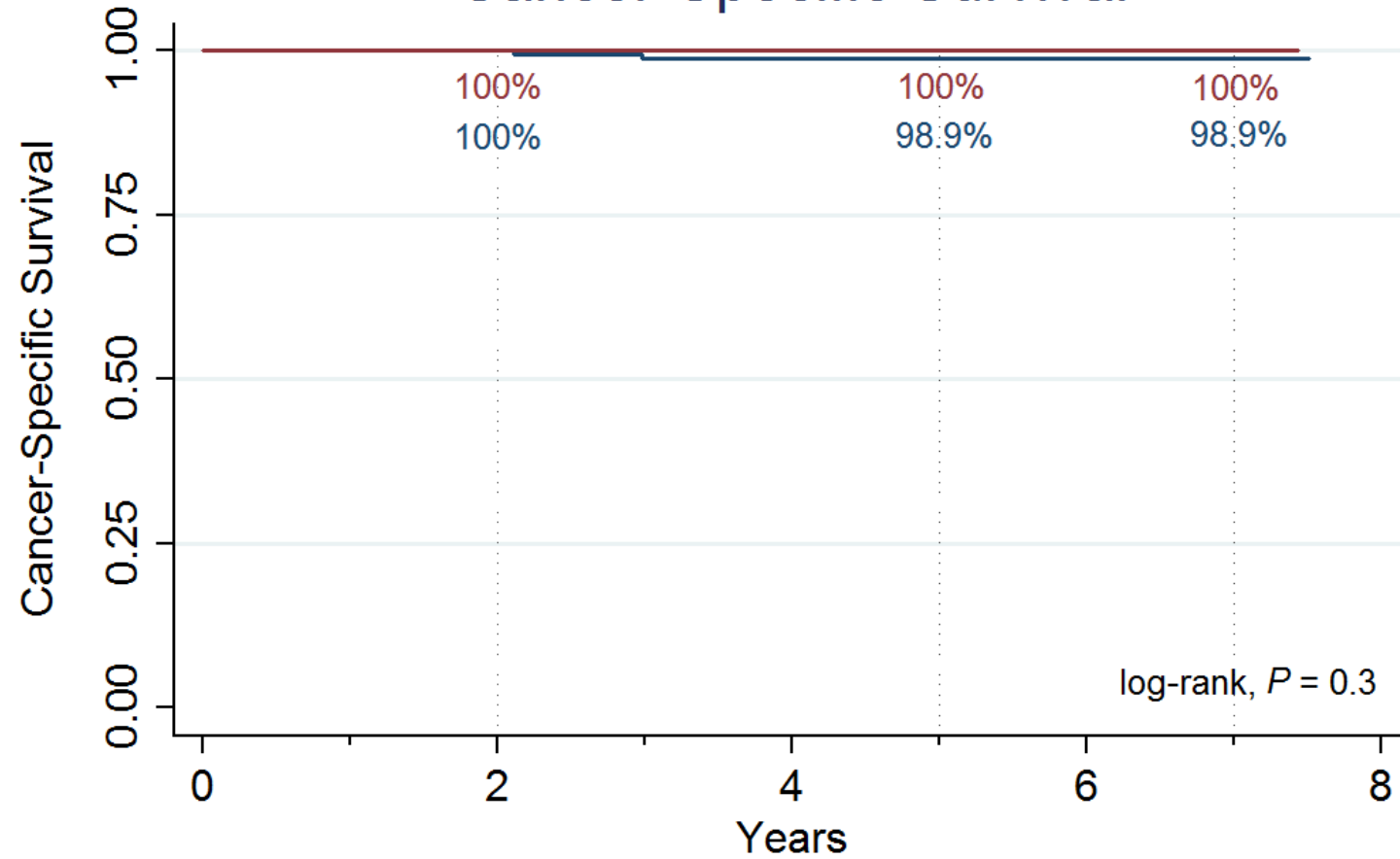
Active Surveillance

Guideline Statement 28-31 (Indications and Protocol)

- For patients with small solid or Bosniak 3/4 complex cystic renal masses, especially those <2cm, **AS is an option for initial management.** (Conditional Recommendation; Evidence Level: Grade C)
- Physicians should **prioritize** active surveillance/expectant management when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of active treatment. (Clinical Principle)
- For patients in whom the **risk/benefit analysis for treatment is equivocal and who prefer AS**, physicians should:
 - repeat imaging in 3-6 months to assess for interval growth and
 - may consider RMB for additional risk stratification. (Expert Opinion)
- For patients in whom the **anticipated oncologic benefits of intervention outweigh the risks of treatment and competing risks of death**, physicians should recommend active treatment.
 - In this setting, AS with potential for delayed intervention may be pursued only if the patient understands and is willing to accept the associated oncologic risk. (Moderate Recommendation; Evidence Level: Grade C)



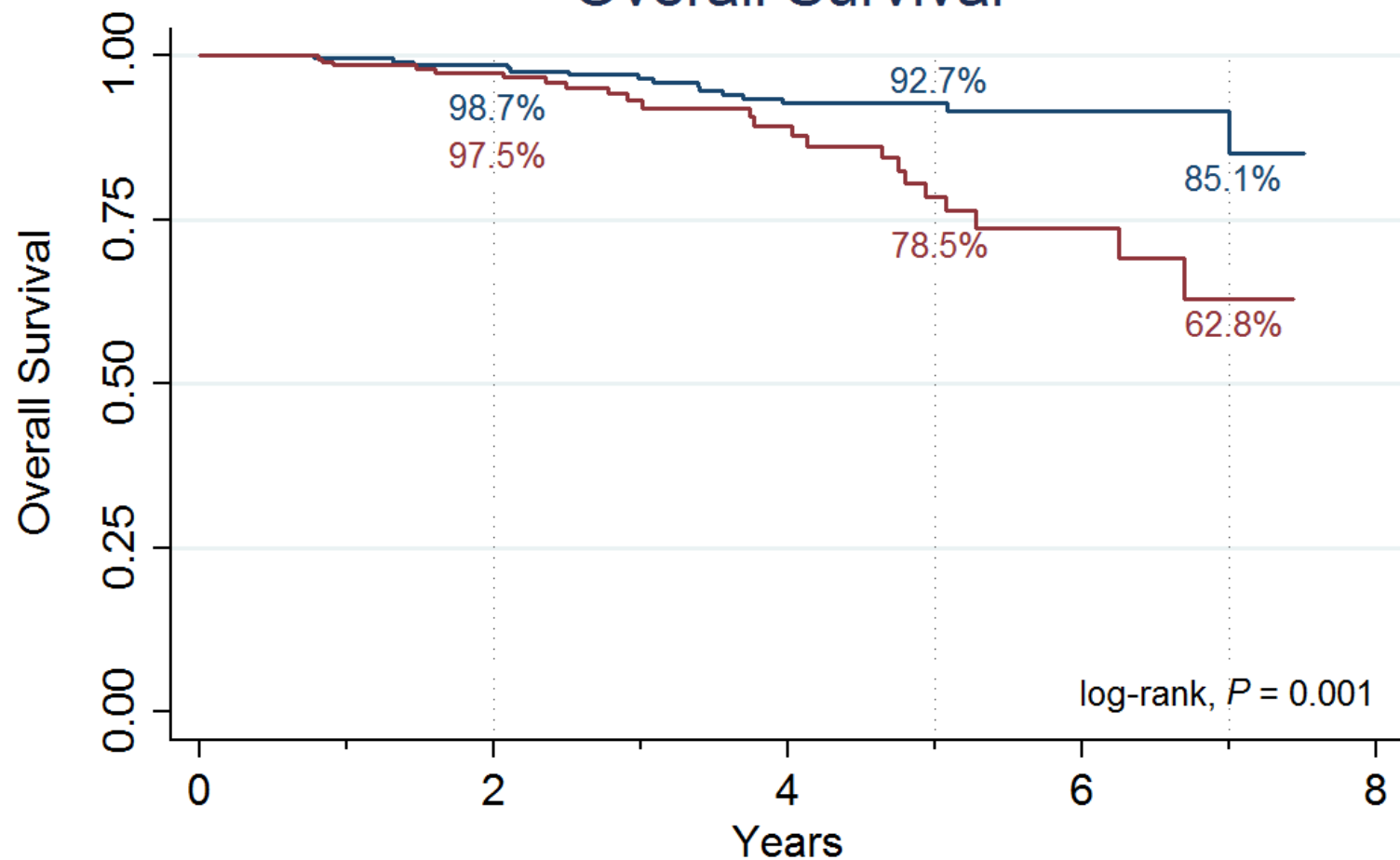
Cancer-Specific Survival



Number at Risk				
Primary Intervention	254	203	130	43
Active Surveillance	285	142	63	21

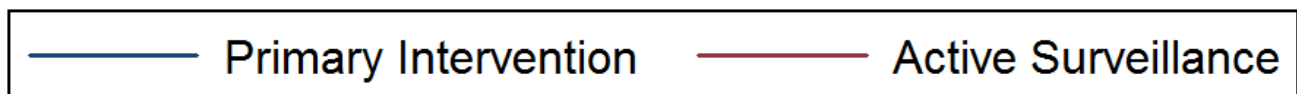
— Primary Intervention — Active Surveillance

Overall Survival



Number at Risk

Primary Intervention	254	203	130	43
Active Surveillance	285	142	63	21



Future directions

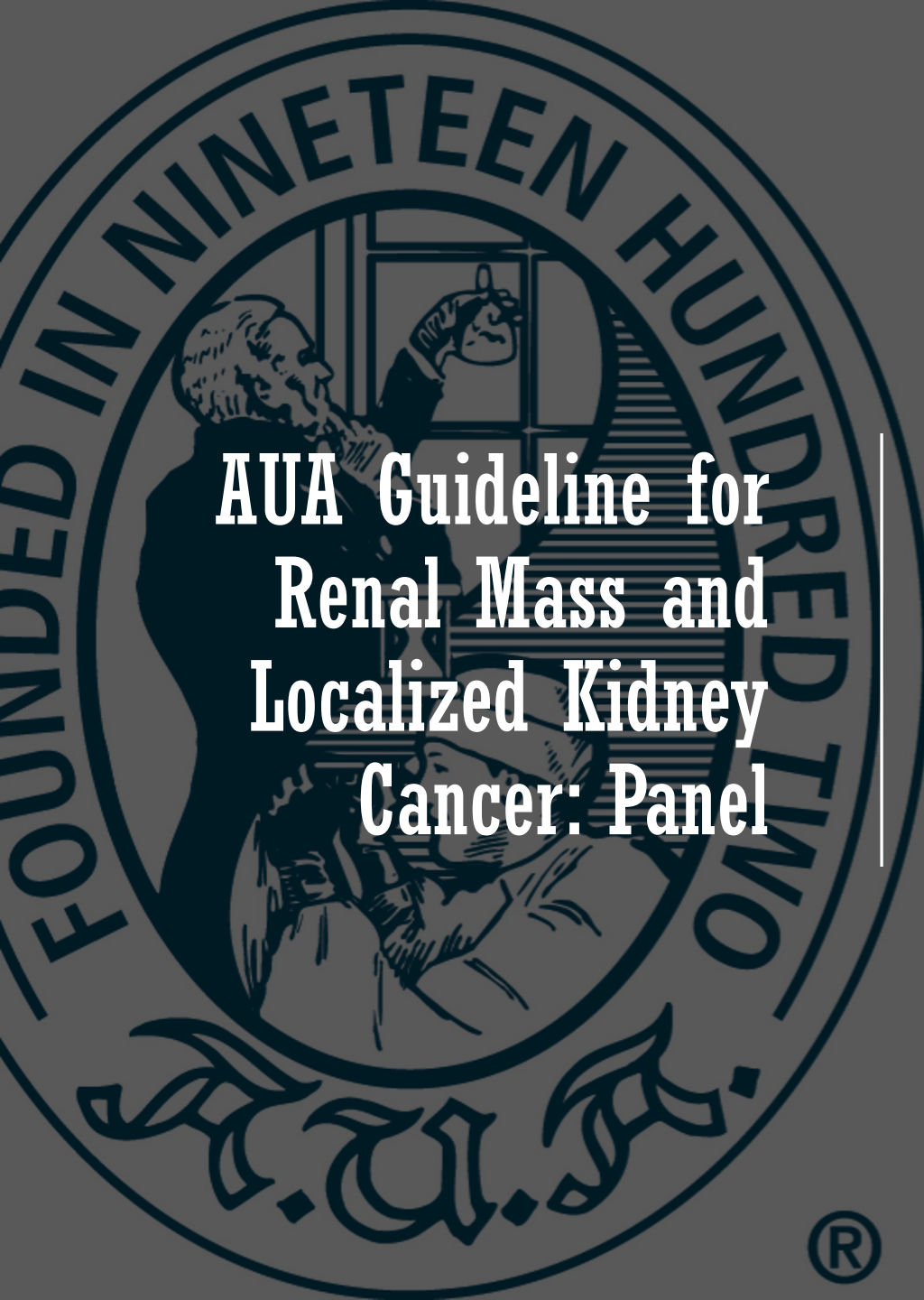
- Evaluation and Diagnosis
 - Molecular Imaging
 - Diagnostic biomarkers
- Counseling and Outcomes-based Research
 - Clinical trials
 - Decision aids
 - Quality metrics
- Management
 - Improved quality of studies
 - Randomized clinical trials
 - Prospective registries
 - Investigational modalities



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- The evaluation and management of clinically localized renal masses suspicious for malignancy involves individual assessment of:
 - Patient characteristics (competing risks of death)
 - Tumor characteristics (oncologic outcomes)
 - Renal functional outcomes
 - Potential harms of each treatment
- Renal mass biopsy is an option when it will influence management decisions.
- Partial nephrectomy is the preferred management strategy for clinically localized renal masses.
- Radical nephrectomy is recommended for tumors with increased oncologic potential in healthy patients.
- Thermal ablation is an option for tumors less than 3cm.
- Active surveillance has a clear role in the management of clinically localized renal masses.
 - An option for initial management in all patients with tumors less than 2cm.
 - Should be customized to individual risk profiles (active surveillance versus expectant management).



The seal of the American Urological Association (AUA) is visible in the background on the left. It is a circular emblem with the text "FOUNDED IN NINETEEN HUNDRED TWO" around the top and "A.U.A." around the bottom. The center features a classical illustration of a man in a suit, possibly a founder, holding a book or document.

AUA Guideline for Renal Mass and Localized Kidney Cancer: Panel

Steven C Campbell, Cleveland Clinic, Panel Chair

Robert G Uzzo, Fox Chase, Vice Chair, representing SUO

Bradley C Liebovich, Mayo Clinic, representing SUO

Peter E Clark, Vanderbilt, member of AUA Guidelines Committee

Mohamad E Allaf, Johns Hopkins, member of AHRQ team

Phillip M Pierorazio, Johns Hopkins, member of AHRQ team

Brian R Lane, Spectrum Health, representing SUO

Jeffrey A Cadeddu, UTSW, representing Endourologic Society

Ithaar H Derweesh, UCSD

Eric Bass, Johns Hopkins, leader of AHRQ

Anthony Chang: U. Chicago, representing College American Pathology

Susie Hu, Brown University, representing American Society Nephrology

Brian J Davis, Mayo Clinic, RT oncology, representing AC Radiology

Debra A Gervais, MGH, ACR and the Society Interventional Radiology

Leo Giambarresi: Patient Advocate